REMARKS

I. Status of the Claims

Claims 1, 2, 4-14, 21, 23-27, 29, 44 and 45 are pending in the application. Claims 1, 2, 4-14, 21, 23-27, 29, 44 and 45 stand rejected under 35 U.S.C. §112, first paragraph for lack of enablement. Claims 1, 2, 4-14, 21, 23-27, 29, 44 and 45 are rejected under 35 U.S.C. §112, second paragraph for indefiniteness. Claims 1, 2, 4-14, 21, 23-27, 29, 44 and 45 are rejected under 35 U.S.C. §102(a) over Peet *et al.* The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

Applicants note that they previously submitted materials relating to this response on December 13, 2001. However, through an oversight, this response was not submitted at the same time. Thus, applicants request that this response be considered in conjunction with the materials previously submitted.

II. Inventorship

The examiner has objected to applicants' attempt to correct the inventorship on the grounds that (a) a signed declaration from Daniel Peet, Jean-Marc Lobaccaro and Joyce Repa is not provided and (b) the fee for the petition was not included or authorized. Applicants respond as follows.

Applicants have provided the additional executed declaration of added inventors Jean-Marc Lobaccaro and Daniel Peet, and a new declaration from the remaining original inventors. Also provided is the consent of the assignee and a petition under 37 C.F.R. §1.48(a).

Applicants need not provide a declaration from Joyce Repa since her removal as an inventor stems from the cancellation of claims. 37 C.F.R. §1.48(b). An appropriate petition setting forth a statement that Dr. Repa's contributions are no longer being claimed is attached.

Applicants previously provided an appropriate check for each of the petition fees.

Thus, applicants renew their request to correct inventorship. First, under 37 C.F.R. §1.48(b), applicants respectfully request that Joyce Repa be removed as an inventor of the instant application. Dr. Repa's inventive contribution is to claims that have been canceled in light of the restriction requirement and subsequent election. Second, under 37 C.F.R. §1.48(a), applicants petition for the addition of Daniel Peet and Jean-Marc Lobaccaro. As outlined in the attached declaration, these individuals made substantial contributions to the conception of the presently prosecuted claims. Third, an appropriate amendment to the application is provided.

III. Rejections Under 35 U.S.C. §112

A. Enablement

Claims 1, 2, 4-14, 21, 23-27, 29, 44 and 45 continue to be rejected under the first paragraph of §112 on the grounds that the specification allegedly fails to provide enablement for the full scope thereof. In particular, the examiner now appears to argue that the sole basis for the rejection is that the claims read on introduction of a dominant negative LXRα mutant. Applicants traverse.

At the outset, applicants are somewhat baffled by the rejection. None of the claims even mentions dominant negative heterologous genes. Thus, the examiner seems to be creating the mere possibility of non-enablement by reference to non-claimed subject matter. This cannot constitute a proper grounds for rejection, and one can ***always*** envision ***some*** non-enabling

situations for a "comprising" claims (*i.e.*, "comprising performing said method on the surface of the sun ....").

Further, the examiner argues, at page 7 of the Office Action, that a mouse having a disrupted LXRα allele resulting in a null mutation or a non-functional LXRα polypeptide is enabled. Looking at each of the independent claims presented, ***that is what is being claimed***. Thus, these claims are acknowledged by the examiner to be enabled. Thus, applicants need not provide any discussion of whether dominant negative mutants exist, or how they might function.

To the extent that applicants believe that they may be misunderstanding the examiner's concerns surrounding this rejection, ***the examiner is urged to contact the undersigned to attempt to resolve this issue***, assuming that all other rejections have been addressed by the submission.

B. Definiteness

The examiner has advanced a series of rejections under the second paragraph of §112. These are addressed below:

Claims 1, 2, 4-14, 21, 23-27, 29, 44 and 45. The examiner first argues that the LXRα allele does not, itself, have the capacity to respond to dietary cholesterol. Applicants have provided an amendment to each of the independent claims to address this issue. Next, the examiner questions what effect a heterologous LXRα would have on a cell. Applicants do not understand the rejection since there is no mention of a heterologous LXRα in any of the rejected claims. Applicants request clarification of the rejection or its withdrawal.

Claims 4 and 5. The examiner has suggested that interruptions occur in the wild-type LXRα allele as the gene includes introns. Applicants have provided an amendment that is believed to address this issue.

Claims 6-9. The examiner argues that the claims are indefinite in that the mutations various mutations are not said to result in the loss of function recited in claim 1. Applicants traverse. To state that the LXRα allele of claims 6-9 fails to encode an active polypeptide is redundant in light of claim 1 – that limitation is carried over into the dependent claims. Claims 6-9 simply specific further structural elements of the LXRα allele. Reconsideration and withdrawal of the rejection is requested.

Claims 10 and 11. The examiner argues that the claims are indefinite in failing to specify that the mutation has an effect. Again applicants believe that stating the effect of the mutation is unnecessary given the limitations of claim 1. Reconsideration and withdrawal of the rejection is requested.

IV. Rejection Under 35 U.S.C. §102

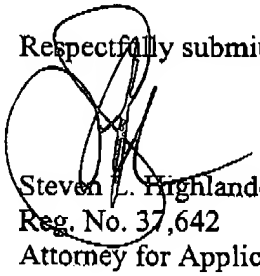
Claims 1, 2, 4-14, 21, 23-27, 29, 44 and 45 stand rejected over Peet *et al.* under §102(a). As discussed above, the inventorship of the instant application should now be corrected. In light of these changes, the only difference between the inventorship of the instant application and the authorship of the Peet *et al.* paper is the inclusion of Ma, Janowski and Hammer as coauthors. As explained in the previously submitted declaration of Dr. David Mangelsdorf, these

individuals did not contribute to the conception of subject matter included in the Peet *et al.* paper, and now claimed in the instant application. Therefore, it is believed that Peet *et al.* is not "by another," and as such, does not qualify as prior art under 35 U.S.C. §102(a). Reconsideration and withdrawal of the rejection is, therefore, respectfully requested.

V. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early indication to that effect is earnestly solicited. Should Examiner Woitach have any questions regarding this response, he is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,



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Date: March 28, 2002

APPENDIX A1 - MARKED UP COPY OF CLAIMS

1. (Twice amended) A transgenic mouse, the cells of which comprise at least one endogenous LXRα allele that [lacks] cannot express LXRα sufficient to provide the capacity to respond to dietary cholesterol.

2. (Twice amended) The transgenic mouse of claim 1, wherein said cells comprise two endogenous LXRα alleles that [lack] cannot express LXRα sufficient to provide the capacity to respond to dietary cholesterol.

4. (Twice amended) The transgenic mouse of claim 1, wherein a transcript produced from said endogenous LXRα allele contains an interruption in the LXRα coding sequence.

5. (Twice amended) The transgenic mouse of claim 2, wherein a transcript produced from said endogenous LXRα alleles both contain an interruption in the LXRα coding sequences.

21. (Twice amended) A method for screening a candidate substance for the ability to reduce cholesterol levels in a mammal comprising:

(a) providing a transgenic mouse, the cells of which comprise at least one endogenous LXRα allele that [lacks] cannot express LXRα sufficient to provide the capacity to respond to dietary cholesterol;
(b) treating said mouse with said candidate substance; and
(c) monitoring a cholesterol-related phenotype in said mouse,

wherein a reduction in said cholesterol-related phenotype in said mouse treated with said candidate substance, as compared to a similar mouse not treated with said candidate substance, indicates that said candidate substance reduces cholesterol levels.

23. (Amended) The method of claim 21, wherein said phenotype is cholesterol absorption, circulating cholesterol, hepatic cholesterol, hepatomegaly, atherosclerosis, cardiac failure, cardiac (atrophy/[hypertropy]hypertrophy), activity level, survival, cancer, reproduction, immune function, skin disease, cognitive function, and adrenal function.

26. (Twice amended) The method of claim 21, wherein said cells comprise two endogenous LXRα alleles that [lack] cannot express LXRα sufficient to provide the capacity to respond to dietary cholesterol.

27. (Twice amended) A method for screening a candidate substance for the ability to increase bile acid synthesis in a mammal comprising:

(a) providing a transgenic mouse, the cells of which comprise at least one endogenous LXRα allele that [lacks] cannot express LXRα sufficient to provide the capacity to respond to dietary cholesterol;
(b) treating said mouse with said candidate substance; and
(c) monitoring a bile acid-related phenotype in said mouse,

wherein an increase in said bile acid-related phenotype in said mouse treated with said candidate substance, as compared to a similar mouse not treated with said candidate substance, indicates that said candidate substance increases bile acid synthesis.

44. (Twice amended) A transgenic mouse cell which comprises at least one endogenous LXRα allele that [lacks] cannot express LXRα sufficient to provide the capacity to respond to dietary cholesterol.

45. (Twice amended) The transgenic cell of claim 44, wherein said cell comprises two endogenous LXRα alleles that [lack] cannot express LXRα sufficient to provide the capacity to respond to dietary cholesterol.

APPENDIX A2 - MARKED UP COPY OF SPECIFICATION

Page 1:

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[Joyce J. Repa]

Daniel J. Peet

Jean-Marc A. Lobaccaro

Stephen D. Turley

and

John M. Dietschy